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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/927,790	08/10/2001	Bassil I Dahiyat	A-67229-9/RFT/RMS/RMK	6955

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EXAMINER

WESSENDORF, TERESA D

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 02/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/927,790	Applicant(s) DAHIYAT ET AL.	
	Examiner T. D. Wessendorf	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3 and 10-18 is/are pending in the application.
- 4a) Of the above claim(s) 10-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 3 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>7</u> . | 6) <input type="checkbox"/> Other: |

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1 and 3 in Paper No. 11 is acknowledged.

Newly submitted claims 10-18 are directed to an invention that is independent or distinct from the elected invention as made in the last restriction requirement, 11/26/02. These claims are the same claims drawn to the non-elected claims, except made dependent on the elected claims. Applicants did not elect claims 10-18. Accordingly, claims 10-18 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Status of Claims

Claims 2 and 4-9 have been cancelled in the Amendment of 1/23/03. Claims 10-18 are added in the current amendment.

Claims 10-18 are withdrawn from consideration, for reasons set forth above.

Claims 1 and 3 are under examination.

Specification

The disclosure is objected to because of the following informalities:

A. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code.

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See page 13, line 13 and line 15. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Applicants are requested to check for other hyperlinks since they are too numerous to mention specifically.

B. The incorporation of essential material in the specification by reference to a publication is improper.

(Specification, page 12, line 10, line 19 and line 24).

Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

Applicants are required to check for other incorporation of essential materials since they are too numerous to mention specifically.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors (typographical, grammatical and idiomatic). Applicant's

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cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 101

Claims 1 and 3 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility.

The specification at page 5, lines 13-24 discloses that the present invention is directed to methods of using computational screening of protein sequence libraries to select smaller libraries of protein sequence that can be used in a number of ways. For example, the proteins can be actually synthesized and experimentally tested in the desired assay, for improved function and properties. Similarly, the library can be additionally computationally manipulated to create a new library which then itself can be experimentally tested. However, creating a library for further screening or testing is not a utility for the method. A library is similar to a composition in nature that has to undergo screening to isolate and identify a product. The court in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful"

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as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . . [i]t is not a reward for the search, but compensation for its successful conclusion. Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing." *Brenner*, 148 USPQ at 696.

Claims 1 and 3 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear,

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concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the enzymes protein design using specific program design, does not reasonably provide enablement for any type of secondary library of scaffold protein variants or sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The scope of enabling disclosure is not commensurate with the scope provided in the specification. The specification, specifically the Examples, disclose a method for generating secondary sequences of specific enzymes utilizing PDA. The rest of the specification discloses nothing more than general description of the claimed method. It is not readily apparent from the disclosure how other protein of secondary structure can be generated from the single example in the specification. While the enabling disclosure is not limited to the working example however, in an unpredictable art such as protein, one

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cannot predict the outcome of a specific protein secondary structure to the vast secondary structure of even a single protein. As a skilled in the art appreciates, to date there are too numerous obstacles for the design of even a single secondary structure of a protein, let alone, all or any kinds of proteins. For example, the combinatorial large number of possible sequences and the incomplete understanding of the factors that control protein structure are still the primary obstacles in protein design. Factors such as helix propensity are important for surface design. Increasing propensity may or may not confer stability on a structure. Changes in the tertiary structure of the protein can occur. Although helix propensity appears to be more important than hydrogen bonding in stabilizing the designed coiled coils, hydrogen bonding could be important in the designing and stabilizing of other types of secondary structure. These limitations are recognized by applicants in the specification' Examples. Amino acid residues are selected such that cys is not used to prevent disulfide formation or Gly that can compromise flexibility and Pro for which an appropriate rotamer is difficult to define. Note further the restriction in the computer design using known primary structure of the known enzyme as obtained

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from the Protein Data Bank wherein water and SO₂ have been deleted to remove any obstacles for its successful design. Therefore, the broad claimed method drawn to any type of protein requires an undue amount of experimentation. While computer protein design holds no barrier or limit, but ultimately the question that needs to be asked, is if such design is feasible in the actual environment where the protein exists. The broad claimed method steps containing too numerous unknown variables are nothing more than an invitation to experiment.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 is unclear as to the method by which a list of primary variant position in the primary library is generated. All libraries at all positions vary since a library is composed

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of all kinds of a.a. of indefinite length and sequences as claimed. The recited "filtered set of scaffold protein primary variants" is indefinite, within the claimed context. The term does not correspond with the specification at page 2, line 19. The specification recites a rank-ordered list of scaffold protein primary variant sequences and not a "filtered set of scaffold protein primary variant sequences". The following terms "primary"; "secondary"; "set" and "plurality" are all indefinite. The arbitrary designations of the library as a primary and secondary library without any differentiating characteristics of its sequences are confusing. The metes and bounds of e.g., the minimum or maximum residues comprised in a set or plurality is not clearly set forth in the claims or specification.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 3 are rejected under 35 U.S.C. 102(b) as being anticipated by Dahiyat et al (Protein Science, 6/1997).

Dahiyat et al discloses, paragraph bridging pages 1333-4, a method using a protein design algorithm for the solvent exposed residues of homodimeric GCN4-pI. The sequences of GDN4-pI display a seven-residue periodic hydrophobic and polar pattern

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called heptad repeat (a, b, d, d, e, f, g). The a and d positions are buried at the dimer interface and are usually hydrophobic, whereas the b, c, e, f, and g positions are solvent exposed and usually polar. The b, c, and f residues positions for surface sequence design are: positions 3, 4, 7, 20, 11, 14, 17, 18, 21, 24, 25 and 28 (filtered set of primary variants, as claimed to create the secondary positions library) were selected. The remainder of the protein structure, including all other side chains and the backbone, was used as the template for sequence selection calculations. All possible sequences of hydrophilic amino acids (D, E, N, Q, K, R, S, T, A, and H) for the 12 surface positions were screened by algorithm. The torsional flexibility of the amino acid side chains was accounted for by considering the discrete set of all allowed conformers of each side chain, called rotamers. Optimizing the residues at positions b, c, and f positions each with 10 possible amino acid results in 10 possible sequences, which corresponds to approximately 10 rotamer sequences when using the Dunbrack and Karplus backbone rotamer library. DEE theorem was used to sequence design that finds the optimal sequence in its optimal conformation.

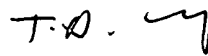
Accordingly, the specific process steps of Dahiyat fully meet the broad claimed method.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
February 9, 2003